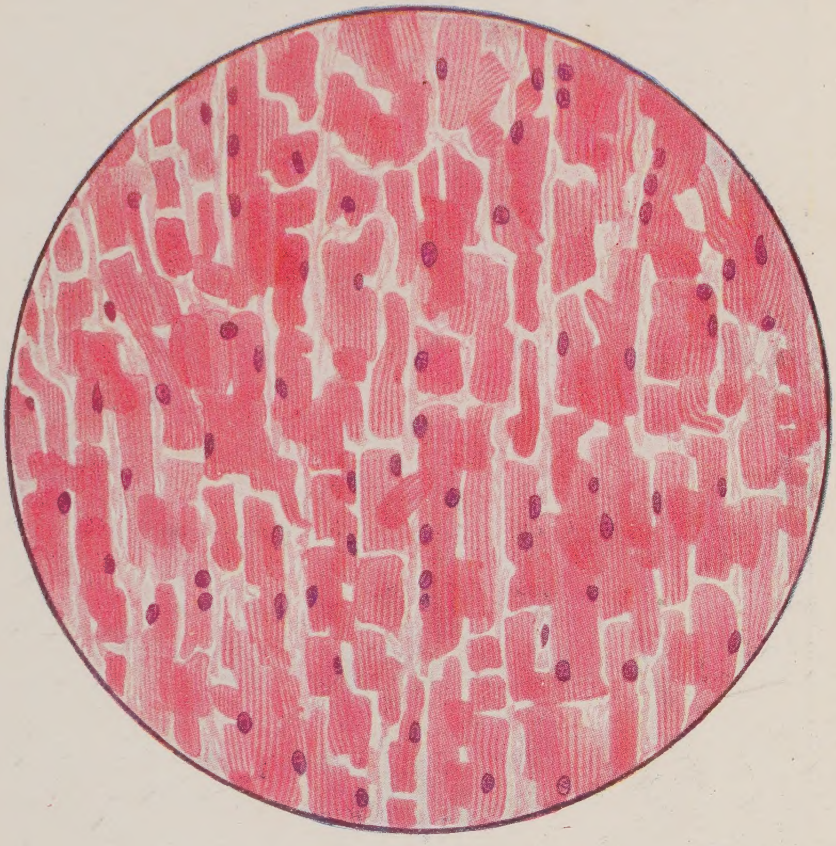
DE MORRHUA

NIL NISI BONUM

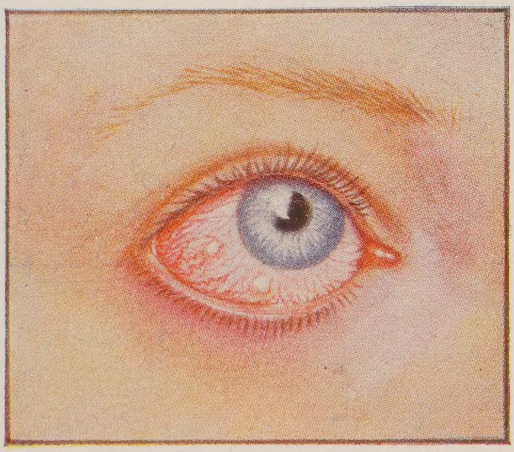
WELLCOME
LIBRARY
pam
QU 160
1936
B97d

BERI-BERI



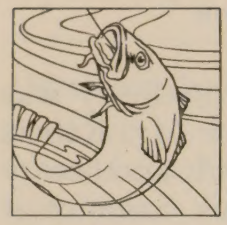
Showing fragmentation and segmentation of the myocardium

PHLYCTENULAR CONJUNCTIVITIS



Two phlyctenules are evident on the conjunctiva

Rib showing site of line of ossification. There is absence of calcification of cartilage and perichondral, and marrow vessels invade the preparatory zone of cartilage. Note osteoid tissue surrounding the invading blood vessels below



Cod fish (gadus morrhua) caught by line

DE MORRHUA NIL NISI BONUM

AS THE title is frankly a modification of the familiar precept *de mortuis nil nisi bonum*, so this booklet is frankly designed to speak well of the value of Cod Liver Oil in medicine.

A certain amount of "Vitamin madness" has developed of late years, and with it a tendency to overlook the fact that it was the established *empirical* value of cod liver oil which led, to a large extent, to an appreciation of vitamin values.

No physician nowadays doubts the value of vitamins, but exaggerated and irresponsible claims by interested manufacturers have tended to obscure the essential importance of their presentation *as factors in natural food products*. For this reason the medicinal uses of cod liver oil and malt are here the subjects of brief historical review.

COD LIVER OIL

There is no authentic record as to the date when the medicinal properties of cod liver oil were first recognised, but it is probable that the Eskimos, the Greenlanders and the Laplanders were acquainted with its remedial virtues during the Palæolithic stage of man's existence long before they came in touch with civilisation. In Norway and Iceland, the oil from the liver of cod has been used from a period of great antiquity. Martiniere, a French traveller in Norway and Lapland in 1674, found it a common article of diet.

The employment of cod liver oil as a medicinal agent in Great Britain dates only from the latter part of the eighteenth century, the recognition of its remedial properties being due to a series of

Printed in England

Raise flap of cover for further illustrations

accidental circumstances. The first discovery was made late in the eighteenth century by Mr. Robert Darbey, who was house surgeon and apothecary to the Manchester Infirmary. In this instance it was used externally and internally, for "a woman who laboured under the most excruciating rheumatism." The encouraging results led to the popularity of cod liver oil for chronic rheumatism, and several years later it appeared in the British Pharmacopœia.

Early use in Rheumatism

In 1782, Dr. Thomas Percival, of Manchester, published a paper entitled "Observation on the Medicinal Uses of the Oleum Jecoris Aselli, or Cod Liver Oil in Chronic Rheumatism and other painful disorders." In this treatise he stated that in the hospital nearly a hogshead of the oil was consumed annually. It was given in obstinate chronic rheumatism, sciaticas of long standing, and in cases of premature decrepitude, repeated strains and bruises or when, owing to exposure to continual dampness and cold, the muscles and tendons had become too rigid, and the flexibility of the joints impaired. The oil of this time was naturally found to be so nauseous and offensive, both as regards taste and smell, that a variety of means were resorted to, to disguise its unpleasant character. In several instances it was found necessary to combine it into the form of a liquid soap, thereby reducing considerably its efficiency.

It was not until after 30 years had elapsed that renewed interest was excited in the medicinal value of cod liver oil, by Dr. S. A. Bardsley, who was a physician at the Manchester Infirmary. He again in the *Medical Report* called attention to the excellent results gained in the treatment of chronic rheumatism by the use of cod liver oil.

First use in Rickets

There is evidence that in 1822 cod liver oil was used in scrofula and rickets by the Dutch medical profession. However, it was used for this purpose by fishermen in Holland for many years prior to this date, although this treatment was not recognised by medical men.

Early in the nineteenth century it was first introduced into France and Germany, but at that period was only used experimentally, and chiefly as an external application. Its use as an internal remedy in pulmonary diseases is incidentally referred to in an article by Drs. Wynne and Thompson in 1847. Mention is there made of the great value of cod liver oil in the treatment of phthisis. The latter physician also stated that he had derived more benefit from cod liver oil in that disease than from any other medicine he had tried.

During 1824–26, there were several definite case-histories of rickets cured by cod liver oil, and later it became generally used throughout Germany for rheumatism, gout, rickets, scrofula and tuberculosis.

Despite the fact that it was found to be so effective, and although it was carefully recorded by reputable and well-known medical writers it fell into widespread disuse. Even in the middle of the nineteenth century, when many physicians were prescribing cod liver oil in the treatment of tuberculosis and rickets, it was stated by many authorities that it was used, not because of any specific values, but only because it was an easily digested and easily assimilated fat. Some authorities refused to recognise any virtues in cod liver oil, and even as late as 1912 still claimed that there was no specific value in the oil. On the other hand, in 1910 Rosenstein claimed that cod liver oil was in the forefront of children's remedies, and in 1908–12 Schabad published his

"Metabolism Experiments," which indicated specific effects in rickets, not produced by other oils.

From this period the beneficial virtues of this natural agent have been proved throughout the world, and its properties as a food as well as a medicine are too well known to need further recapitulation. Its combination with malt prepared from barley, one of the most nutritious grains known to man, is an ideal combination, of which time has proved the value.

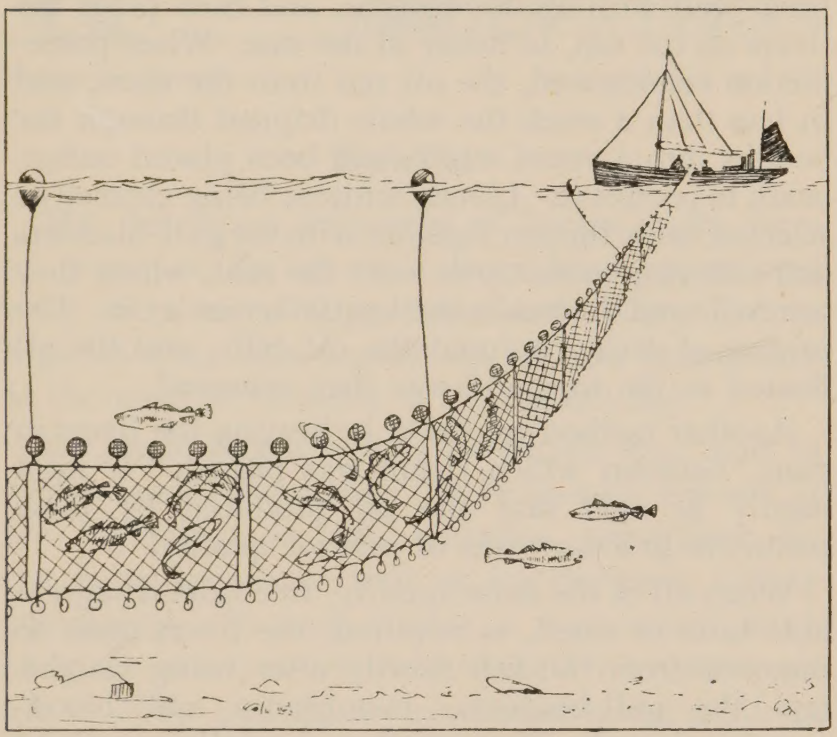
Cod Fisheries

There is evidence that, as early as the ninth century, the Vestfjord fishers were in existence, and also that the famous Lofoten Islands constituted the leading stations. The visits of the cod to the shores of these islands are mentioned in Eigil's Saga, which dates from A.D. 930.

The Iceland trade and fishery is frequently mentioned in ancient records, and probably embraced, as the Newfoundland fishery did in later times, a much wider area than the name implied. The fishermen frequently brought their products to Westmaney, not only from Gunnbeorns Skerries and the East Coast of Greenland, but also from Wardhouse, beyond Cape North, and from the Lofoten Islands. The extent and ramifications of the trade and exchange carried on in Iceland and the adjacent seas, and England's share in it, are unfortunately little mentioned by historians. The Newfoundland cod fisheries were founded after Cabot's discovery of the island in 1497, and, in 1578, according to Hakluyt, four hundred vessels were engaged in the trade. Then, a few years after Cabot had spread news of the abundance of fish, the French fishermen of Normandy and Brittany, who have always been renowned for their courage, ventured across the Atlantic in their small fishing boats.

Huxley describes the coming in of the cod on the coast of Norway as one of the most wonderful

sights of its kind in the world. The fish form what is called a "gods' mountain" of a depth of 120 to 180 feet, and the fishermen, when they let down their loaded lines, feel the lead knocking against the bodies of the fish for a long time



Net fishing for cod

before they reach the bottom. The shoals appear at the Lofoten Islands about the first week in January, and the fishermen commence work, which continues till April, and during that period an immense number of fish are caught by long line, hand and net. The nets are fitted with floats and sinkers, and, as the cod prefer a certain temperature, these nets are let down to the depth at which this temperature exists. After April, the fish go further north, to Finmarken, where the fishing continues until the end of May or even June.

Preparation of the Oil

For centuries the oil was extracted from the livers of the cod in a very primitive way. In 1757, it was recorded that the oil was extracted from the fish livers by heating them in large iron vessels. Another method was to punch a hole in a tub, lined well with spruce boughs, and then place the livers on the top, to decay in the sun. When putrefaction commenced, the oil ran from the mass, and in less than a week the whole dripped through the boughs into a vessel which had been placed underneath to receive it. Livers, without being cleaned or selected, were thrown together with the gall-bladders and adhering membranes into the tubs, where they were allowed to remain until putrefaction set in. The process of decay ruptured the oil cells, and the oil floated to the top, and was then removed.

Another method consisted in heating the livers in pans, between which steam was passed. It need hardly be said that the oil produced by these primitive processes was of inferior quality.

When oil of the finest quality, free from disagreeable taste or smell, is required, the livers must be removed from the fish shortly after being caught, and the gall-bladders, membranes and blood-vessels rejected. They are then carefully examined and the perfectly healthy livers only are selected, and these are thoroughly cleansed by repeated washings. After this process, the livers which exhibit nothing but pure, fresh, fatty tissue are ready for the extraction of the oil.

During this extraction, the oil is kept from exposure to the air, and the whole process is carried out under conditions of absolute cleanliness. By the final refining, a pure, limpid, non-freezing oil is secured, of the highest possible grade, which, by means of cold storage, is preserved in the finest condition, until it is required.

Reaping and Gleaning — From a XIII Century MS.

Barley

The demulcent properties of barley in the form of ptisan or barley-water have been appreciated since the time of Hippocrates and Galen, and its high dietetic value continues to win encomiums in the medical treatises of the present day.

In Anglo-Saxon times, barley-ale was held in high repute medicinally. It frequently appears as an ingredient in the remedies prescribed for the more serious as well as for the most trifling complaints. In lung disease, a man is to "drink clear ale and is to withhold himself from sweetened ale." Fever patients are recommended to drink an infusion of clear ale, wormwood, githrife, betony, bishop-wort, marrubium, fen-mint, rosemary and other herbs. It was also used for many minor ailments, such as hiccough.

From the records of St. Thomas's Hospital (London, Eng.) (1570–1574) we learn that "in consideration of the hote tyme of the yeare the poor shall have allowed every-one a day three pyntts of bere for two months."

Hart, in a work on the diet of the diseased, published in 1633, states that in his time, "ptisan

was called cream of barley, for it serveth the sicke instead of both meat and drinke. Barley for the sicke was alwaies in the highest esteeme."

The value of barley as a foodstuff has been proved to be much enhanced by the process of malting, which leads to the formation of diastase and maltose. To these two products—the one as a digestive, the other as a nutrient—the food value of a properly-prepared extract of barley malt is mainly due.

'KEPLER' MALT EXTRACT is prepared solely from the highest grade winter-malted barley, and is at every stage of production under the most skilled scientific supervision.

It contains the important food-principles—carbohydrates, albuminoids and salts—while non-essential material is eliminated. 'KEPLER' MALT EXTRACT, prepared as it is from diastatic malt extract, provides not only a food of high nutritive value, but contains diastase in adequate proportion.

Diastase and maltose are present in proportions which experience and research have indicated as most serviceable for dietetic and medicinal purposes. Malt extracts of unusually high diastatic power have been shown to be correspondingly weak in the very important nutritive constituent maltose, while those overloaded with maltose lack the digestive properties due to a proper diastatic content.

Its combination with the finest cod liver oil, as in 'KEPLER' COD Liver Oil with MALT Extract, produces a food which contains natural nutrients of high dietetic and calorific value. As will be seen later it also presents in their *natural* form and association Vitamins A and D, in association with Vitamin B complex, in the natural proportions in which they are provided by Nature.

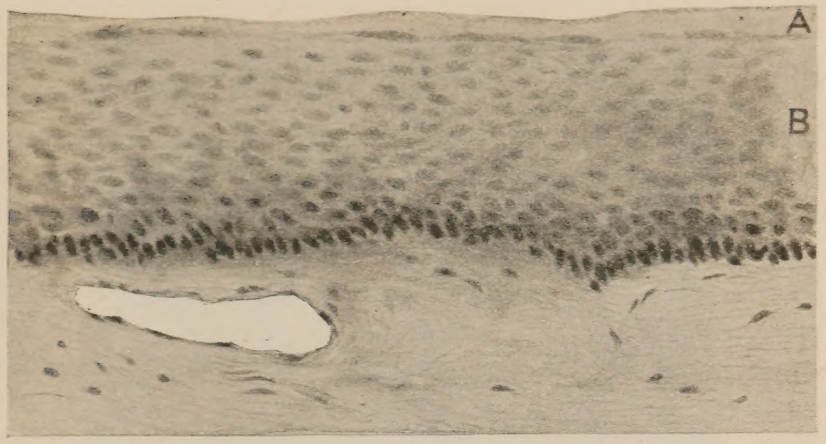
VITAMINS

The discovery, in 1880-81, by Lunin, that an unknown factor necessary for growth in animals was lacking in synthetic milk diet may be said to be the starting-point in the revival of interest in the problem of nutrition and the first milestone in the recent knowledge of accessory food factors or vitamins. In 1897, Eijkman, stimulated by the success of Takaki (1882–86) in eradicating beri-beri from the Japanese navy by the introduction of an improved mixed diet, made the first tentative experiment when he fed pigeons on a diet restricted to milled or polished rice and found that they developed a condition of paralysis (polyneuritis) strikingly like beri-beri in man. He suggested that there was something in the bran layer which protected against this pathological condition. In 1901, Grijns confirmed Eijkman's findings of the presence of this anti-neuritic substance in rice husks and beans, and, in 1907–9, Fraser and Stanton successfully treated experimental polyneuritis with an alcoholic extract of rice-polishings. In the same year, Funk called attention to these and other experiments which indicated the existence of an indefinite group of substances in food which were indispensable to complete health, and suggested the word "Vitamine" to denote the missing necessary factor in the polished rice production of beri-beri. He attempted to isolate this missing factor from the pericarp and postulated vitamin deficiency for beri-beri, scurvy, pellagra and rickets. This led to a widespread investigation into the results of feeding laboratory animals on diets of varied types and constitutions.

Beginning of Modern Conception of the term Vitamin

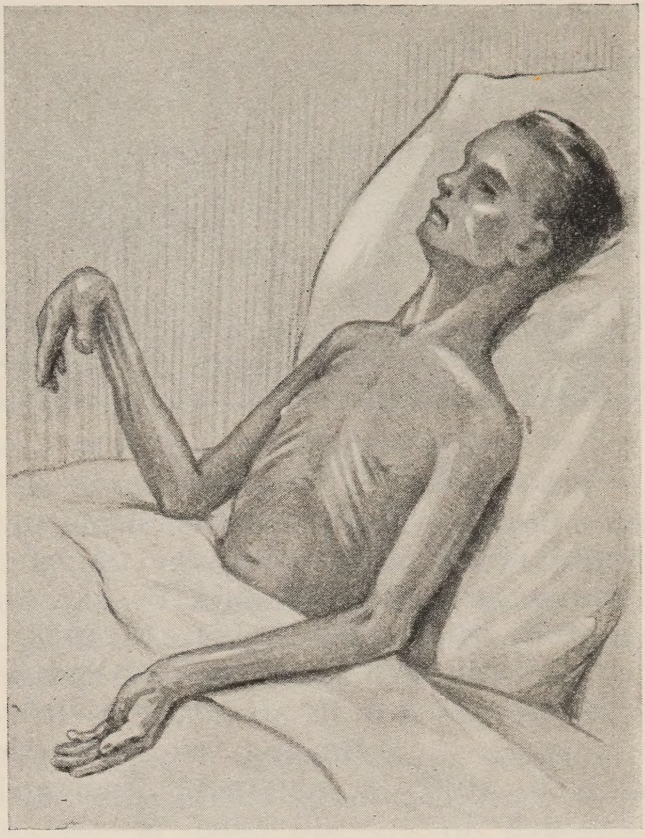
In 1912, a year of outstanding importance in vitamin research, Hopkins published the results of a long investigation, carried out over a number of years, which gave conclusive experimental proof of the existence of unknown and indispensable substances in diet. He demonstrated that laboratory animals could not live on a purified well-balanced diet of correct energy value unless a small quantity of fresh milk was added each day : thus confirming the earlier experiment of Lunin. Hopkins termed the necessary dietary substances "accessory food factors." Even as early as 1906 he had written with reference to possible missing nutritive principles in diet, but it was the publication of his work in 1912 that marked the beginning of a full and proper appreciation of these dietary factors that we now term "vitamins."

Following Stepp's experimental evidence (1909–12) of the existence of some indispensable dietary unit associated with lipoids, McCollum, Davies and Kennedy (1912–16) accumulated data to show that butter-fat, dissolved out with ether, secured prolonged growth in animals when added to diets which would not otherwise support growth. Egg-yolk fat was found to have the same property, but the addition of lard and olive oil to the diet resulted in little growth and early failure. Fat-soluble Vitamin A associated with certain fats was thus first recognised. It was realised, however, that there was not one but a series of essential dietary principles. Further researches by many workers have been directed to the identification and isolation of these accessory food factors. The recognition of Vitamin A was followed by the identification of water-soluble Vitamin B, never associated with fats, but widely distributed in vegetable foods.



Keratinisation of the corneal epithelium
due to Vitamin A deficiency
A—Keratinisation B—Thickened Epithelium

Evidence further accumulated to show the existence of a third factor necessary to the life of certain animals—water-soluble Vitamin C. It was first suggested by Holst and Frölich, in 1913, as the missing factor in diets producing scurvy, and Hess (1914–18) showed it to be abundant in citrus fruits and tomatoes. Following the extraction by Windaus in 1917 of cholesterin from cod liver oil, research in the direction of the relation between bone growth in the young and diet established the identity of Vitamin D (1922) which usually occurs in association with Vitamin A. Experimental rickets, by a dietetic deficiency, was produced in puppies by Leonard Findlay in 1908, and in rats by McCollum and Simmonds in 1917–21; but it was not until 1918–19 that Mellanby demonstrated the marked improvement in such cases following the administration of cod liver oil. The effects of cod liver oil on the deposition of calcium on the bones and the increase of phosphorus in the blood were demonstrated by Howland and Park in 1920. A fat-soluble Vitamin E, which is said to be necessary for reproduction in certain animals, was recognised by Evans and Bishop in 1922–23.



VITAMIN B DEFICIENCY
Dry Beri-beri showing typical paralysis (wrist-drop)

Studies are now being directed towards the elucidation of the chemical structure and nature of the vitamins and their isolation and concentration in a free state apart from the association in which they naturally occur. Considerable progress has been made in this direction, but the complexity of Vitamin B and the possible dual nature of Vitamin D indicate that much work has yet to be done.

Synthesis of Vitamins by Plants

Animals are, in general, dependent for their vitamin supply on the contents of the diet. (The rat can synthesise Vitamin C, and Vitamin D is

produced in the skin of animals by sunlight.) The vitamins stored in the tissues or available for use in any animal are supplied directly and in quantitative proportion by the diet of that animal. The ultimate source of vitamins, therefore, is seen to be in the chlorophyll-containing plants, in which it seems that the process of photosynthesis is accompanied by the production of vitamins. The more highly differentiated forms of animal life are not dependent on light for the functioning of their fundamental processes of metabolism, although light can still affect some of their cells. But such higher forms have become dependent on a series of chemical substances for the formation of which light is necessary. Marine animals are no less dependent on this source than are land animals. The vast supply of microscopic algæ and diatoms possessing photo-catalytic pigments form the source of food and vitamin supply for the larger animal plankton, such as the copepods and other entomostraca. These latter form the food for the young and smaller fish, and these again the food of larger fish. The ultimate source, therefore, of the vitamins contained in certain fish oils, such as cod liver oil, is represented by the free floating microscopic plants on the ocean surface.

Natural Vitamin Products or Concentrates

Research in regard to the vitamins has revealed their complicated nature. This is particularly evident with regard to irradiated ergosterol (calciferol), the most firmly established of all vitamin concentrates, as it is now reasonably certain that it is not identical with the Vitamin D obtained from animal sources. The available evidence* clearly indicates that ergosterol is not the only naturally occurring precursor of an anti-rachitic

* Edgar Stedman : Reports of the Progress of Applied Chemistry, xx, 665, 1935.

substance, and that the anti-rachitic activity of cod liver oil is due to a substance which is different from, although perhaps related to, calciferol. Thus, it is not surprising that there is a growing mass of evidence in favour of natural vitamin-containing products. The potency of vitamin concentrates and the knowledge that over-dosage may cause injurious effects to the body have tended to encourage the movement towards natural vitamin-containing products such as cod liver oil. The value of cod liver oil is unquestioned, and there can be little doubt that the difficulty associated with its administration is overcome when cod liver oil is presented as a palatable food product. Concentrates have practically no calorific value and depend solely on the presence of the vitamins. They are, therefore, of value only when vitamin deficiency exists.

Where rickets already exists, for instance, calciferol must undoubtedly have its place, but it is in the prevention of such diseases as rickets that the addition to the dietary of the growing child of a natural food substance, such as cod liver oil, is indicated. It is not unreasonable to state that growth and health must depend very largely on nutritious food and that the products of the laboratory should be reserved for the treatment of disease. Even halibut liver oil must be regarded only as an important supplement to, rather than a substitute for, a good cod liver oil. The liver oil of the halibut is especially rich in Vitamin A, but considerable variation occurs in the amounts present, while the oil is relatively poor in Vitamin D. It is, therefore, necessary to reinforce its Vitamin D content by artificial means. Further, cod liver oil presents not only Vitamins A and D in requisite proportion and amount, but also an easily assimilable fat which

constitutes a valuable food; this is negligible in halibut liver oil in the quantities in which it is administered. If halibut liver oil were administered in doses sufficiently large to present any fat value, hyper-vitaminosis would soon be apparent and the results might be serious. Similarly, tuna oil is of little food value and, in addition, is of such potency that, following its administration, undesirable after-effects are a constant danger unless used with extreme caution.

Cod liver oil is usually administered in combination with malt extract and is thus presented in a palatable form free from all nauseating taste and odour. Cod liver oil is a food rather than a drug, and is the most easily assimilable of all oils. It increases weight and improves the general condition of the patient, being often well borne by those not able to digest fats. The medicinal virtues of the oil are due in the main to the relatively large amounts of Vitamin A and Vitamin D in their natural form and association, together with the valuable iodine content of the oil. The iodine content, which varies considerably in amount in different oils, was first detected by Hupper de l'Orme in 1836.

Although the following extract* was written with special reference to the diet in gastric diseases it undoubtedly represents the trend of modern thought with regard to diet in general.

> "With regard to the Vitamins, A and D are more likely than the others to be deficient, and particular attention should be paid to their adequate supply. In any ordinary mixed diet, B and C will be plentiful. I think it is well to be moderate in the use of all these substances, and I am not sure that they are not too freely used generally. Animal experiments show that extraordinarily minute quantities are sufficient to

* *Post-Graduate Medical Journal*, March, 1935, *page* 106

maintain health; and the quantities found in their natural sources are also minute. It would seem, therefore, that large quantities of vitamins are not necessary, and there is no evidence that they are desirable. It has already been shown that it is quite possible to give too much Vitamin D and that ill-effects follow its excessive use. Doubtless before long similar demonstrations will be made in the case of other vitamins. I suspect that in the near future it will be definitely shown that the amount of vitamin taken should be of the same order as occurs in nature; and that most, or all, of the concentrated products now commonly used are, at any rate, potentially, harmful."

Further, it has been pointed out* that young infants may have an idiosyncrasy to Vitamin D and that, therefore, the present day tendency to increase the Vitamin D potency of cod liver oil is undesirable and unnecessary.

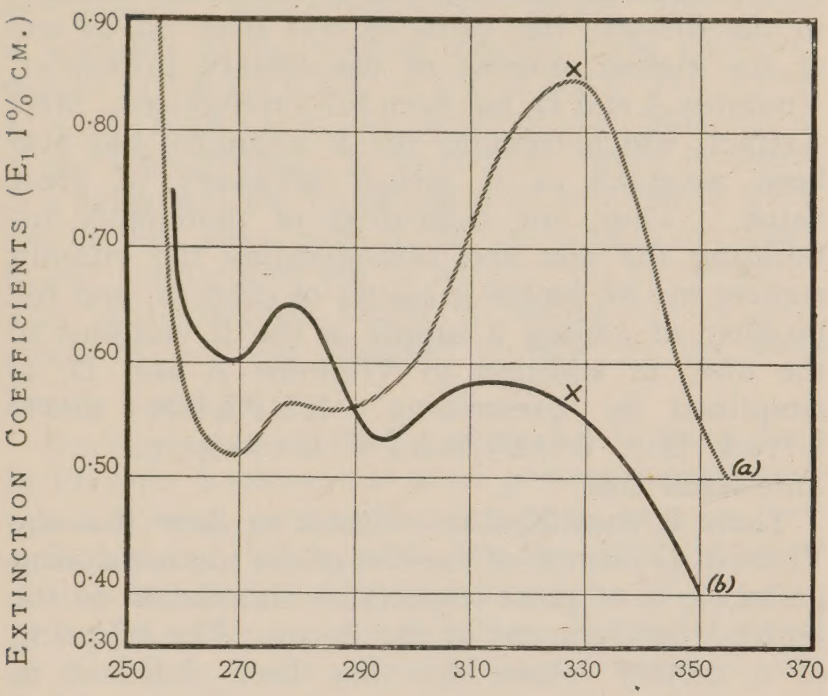
Vitamin Therapy

The most useful classification of the vitamins would appear to be one indicating their chief clinical uses, as follows:—

Fat-Soluble A	—The growth or anti-xerophthalmic vitamin.
Fat-Soluble D	—The anti-rachitic vitamin.
Fat-Soluble E	—Fertility or anti-sterility vitamin.
Water-Soluble B_1 or Vitamin F	—Essential for growth: Deficiency leads to beri-beri in man and poly-neuritis and beri-beri in pigeons.
Water-Soluble B_2 or Vitamin PP, or Vitamin G	—Together with B_6, the pellagra-preventing vitamin.
Water-Soluble B_3, B_4, B_5	—These are ill-defined growth factors.
Water-Soluble B_6	—The anti-dermatitis vitamin.
Water-Soluble C	—The anti-scorbutic vitamin.

* Lewis Thatcher, *The Lancet*, I, 20 (Jan.), 1936

A Chart of the Ultra-Violet Absorption Curve of Cod Liver Oil



For the spectrographic estimation of the Vitamin A content of cod liver oil an absorption curve, in which extinction coefficients (E) are plotted against wave-lengths, is drawn from measurements made in the ultra-violet region of the spectrum with a quartz spectrograph. A 1 per cent. solution of the oil in alcohol is usually examined, and the above illustration shows curves obtained, using a typical 'Kepler' Cod Liver Oil *(a)* and an old sample of oil which had deteriorated *(b)*. The well-marked absorption band with a maximum at wave-length 328*mμ* is due to Vitamin A, and the extinction coefficient at this wave-length is regarded as being proportional to the amount of Vitamin A present in the oil. The estimation of Vitamin A by this method, which has been used for the examination of 'Kepler' Cod Liver Oil for some years, was recently afforded official recognition by the Second International Conference on Vitamin Standardisation *(see Lancet*, 1934, II., 45).

Therapeutics of Cod Liver Oil with Malt Extract

Ever since the introduction of modern methods of food production necessitating revolutionary changes in the dietary, the value of cod liver oil as one of the richest sources of the dietary principles, Vitamins A and D, has been fully recognised. Malt Extract, which contains the B vitamins, has also been accepted as a dietary accessory of great value. Thus, the difficulties of thoroughly re-building the diet and safe-guarding the vitamin content are no longer a matter of concern, and the problem of adding a supply of the B vitamins to the diet, in addition to Vitamins A and D, is simplified by prescribing 'KEPLER' COD LIVER OIL WITH MALT EXTRACT.

Ante-Natal Use

There is considerable evidence to show that the Vitamin D content of the diet of the mother during gestation is of great importance in relation to the skeletal development of the fœtus. The offspring of a mother whose diet has been deficient in Vitamin D is often predisposed to rickets, of low general vitality and with teeth of poor development. Further, Mellanby has pointed out that most of the ordinary foodstuffs are so iodine-deficient that they do not afford sufficient supply for the mother to pass on to the developing embryo, with the result that the thyroids of the offspring become hyperplastic. During the ante-natal period the provision of a full Vitamin D supply in the diet, together with the beneficial iodine content of cod liver oil, is simplified by the use of 'KEPLER' COD LIVER OIL WITH MALT EXTRACT supplemented, in extreme cases of Vitamin D deficiency, by daily doses of 'TABLOID' CALCIFEROL.

The vitamin content and other qualities of the milk depend on the diet of the mother during lactation. The vitamins present in the milk

vary quantitatively with the amounts in the diet. Breast-feeding is not an insurance against rickets or general hypovitaminosis unless the milk is complete in its vitamin content. The administration of 'KEPLER' COD LIVER OIL WITH MALT EXTRACT, in doses of one teaspoonful to one tablespoonful, to the mother during lactation is a safeguard the physician may adopt with good results. In some cases it may be thought necessary to add a daily dose of 'TABLOID' CALCIFEROL. The anti-scorbutic factor (Vitamin C) is provided by a daily addition of fruit to the diet.

During Lactation

During lactation, the requirements of the mother in Vitamin B are several times greater than at other times. What previously may have been a bare sufficiency of Vitamin B in the diet becomes, during lactation, a definite deficiency. 'KEPLER' MALT EXTRACT, is, therefore, of special value at this time. *See also* Calcium Gluconate and Iron, *page* 27.

Reduced facsimile

All 'Kepler' Cod Liver Oil is tested for Vitamin A by the most practicable method, and the results are confirmed from time to time by the growth test on rats. All 'Kepler' Cod Liver Oil is tested for its content of Vitamin D in accordance with the method of the Medical Research Council. The B vitamins are invariably present in 'Kepler' Malt Extract.

'Kepler' Cod Liver Oil with Malt Extract has been kept at room temperature for 12 months, after the removal of some of the contents of the bottle, without any evidence of decline in vitamin activity.

'KEPLER' MALT COMBINATIONS

For use in various nutritional disorders, in addition to 'KEPLER' COD LIVER OIL WITH MALT EXTRACT, the following 'KEPLER' combinations are also available:—

TRADE MARK 'KEPLER' COD LIVER OIL WITH MALT EXTRACT AND IRON IODIDE

When combined with 'KEPLER' COD LIVER OIL WITH MALT EXTRACT, iron iodide is protected from rapid oxidation, the malt extract serving as an efficient vehicle. The hæmatinic properties of the iron iodide are associated with the rich vitamin content of the 'KEPLER' COD LIVER OIL WITH MALT EXTRACT (Vitamins A, B and D), which is indicated even when all other essential components of a diet are present, as there is abundant evidence to show that serious detrimental effects on all the tissues of the body may result from deficiency of iron. Anæmia, growth failure and a general loss of condition are the outstanding effects in such cases. The addition, therefore, of small doses of iron to the diet of the young and growing child is not only rational but is of particular value in preventing anæmia of early infancy. Therefore, as the human infant has no large store of iron and receives very little in its food, it has been advocated* that every baby, whether breast- or artificially-fed, for the first six to nine months of its life would benefit considerably by the addition of iron to its diet.

TRADE MARK 'KEPLER' COD LIVER OIL WITH MALT EXTRACT AND CHEMICAL FOOD

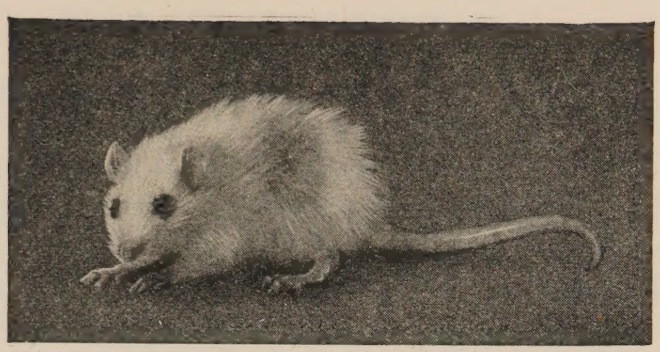
Chemical Food *(Phosphates Compound)*, an excellent general tonic for children and adults, is here presented in a most palatable form.

TRADE MARK 'KEPLER' COD LIVER OIL WITH MALT EXTRACT AND CREOSOTE

In this preparation the therapeutic efficiency of creosote is augmented by presence of cod liver oil.

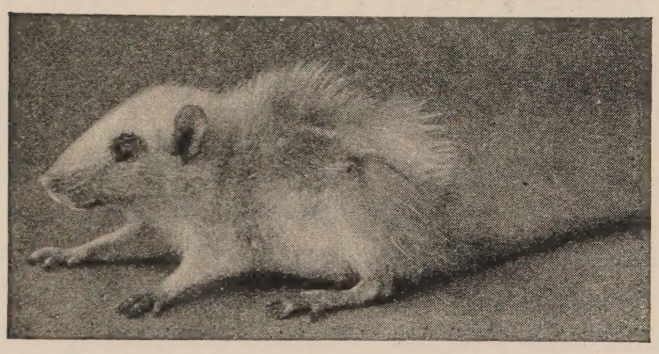
* *British Medical Journal*, April 29, 1933, *page* 742

RAT 1



RAT 2

RAT 3



RAT 4

RATS 1, 2 and 3.—Fed on diet devoid of Vitamin A. Show xerophthalmia, rough coat and general lack of condition.

RAT 4.—Fed on same diet as its litter mates, Rats 1, 2 and 3, but with the daily addition of 8·3 mgm. of 'KEPLER' COD LIVER OIL WITH MALT EXTRACT

TRADE MARK 'KEPLER' COD LIVER OIL WITH MALT EXTRACT AND HYPOPHOSPHITES

The hypophosphites are unstable and deliquescent salts. They are best presented in conjunction with 'KEPLER' COD LIVER OIL WITH MALT EXTRACT which conserves their chemical properties and masks their unpleasant taste.

TRADE MARK 'KEPLER' MALT EXTRACT WITH GLYCEROPHOSPHATES

'KEPLER' MALT EXTRACT provides an ideal vehicle for the administration of the glycerophosphates of calcium, potassium, sodium and magnesium. This combination is very acceptable when taken with milk.

TRADE MARK 'KEPLER' MALT EXTRACT WITH HÆMOGLOBIN

'KEPLER' MALT EXTRACT WITH HÆMOGLOBIN contains gr. $9\frac{1}{5}$ (0·596 gm.) 'WELLCOME' Brand Hæmoglobin in each fluid ounce. In this form the hæmoglobin is without irritant action.

ACCESSORY PRODUCTS

TRADE MARK 'RYZAMIN-B' BRAND

RICE POLISHINGS CONCENTRATE

'RYZAMIN-B,' which consists of the concentrated and purified vitamin-containing fraction of rice polishings (recognised as a rich source of Vitamin B_1), has a potency of not less than 50 International Units of Vitamin B_1 per gramme. Thus it is possible to add to the diet an adequate supply of the anti-neuritic factor in a relatively small bulk (1/2 gramme, or about 1/16th teaspoonful). Doses of Vitamin B, which could not be tolerated by many patients in the form of yeast concentrate, may thus be given with safety.

Vitamin B_1 is stated to promote appetite, to aid digestion and to bring about increased tonicity and absorptive powers of the digestive tract; it stimulates the general metabolic processes, promoting growth,

and acts as a valuable prophylactic against polyneuritis. Further, it is stated to be necessary for normal reproduction and lactation.

Severe Vitamin B_1 deficiency, such as occurs in beri-beri, sprue, polyneuritis and allied conditions, presents definite and readily recognisable symptoms; when the deficiency is mild or partial, however, the signs are much less marked and their significance may not be apparent. Many observers have noted that loss of appetite is an almost invariable accompaniment. Kruse and McCollum* state: "Outstanding among the symptoms of Vitamin B deficiency is anorexia."

In infants there may also be impairment of the digestive processes, intestinal atony, loss of weight and vigour, and lack of growth, especially during the breast-feeding period. Irritability, lack of appetite, fretfulness of infants and young children, and failure to gain in weight, are due in many cases to Vitamin B deficiency, and can be corrected by adding B vitamin-containing food to the diet.†

Marasmic babies have their interest in food and appetite restored by administration of Vitamin B; insufficient anti-neuritic vitamin is more serious in children than in adults, by reason of the child's lowered capacity for tissue-storage of vitamin reserve and greater need to meet growth requirements.‡ Shortage of Vitamin B can be a factor in limiting the growth of school children.§

FURTHER INDICATIONS

Very large doses of potent Vitamin B preparations are of use in the peripheral neuritis of chronic alcoholics.|| It has been stated that the polyneuritis of pregnancy is probably a dietary deficiency

* *Journal American Medical Association*, H. D. Kruse and E. V. McCollum, 98:2201 (June), 1932.
† *Journal American Medical Association*, August 4, 1928.
‡ *Journal American Medical Association*, George R. Cowgill, 98:2282 (June), 1932.
§ *American Journal Diseases of Children*, May, 1930.
|| *Yale Journal of Biological Medicine*, 1933, 6, 75.

disorder similar to beri-beri and that large doses of Vitamin B concentrates are indicated.*

'RYZAMIN-B' is suggested, primarily, as a dietary reinforcement for patients of all ages, to stimulate appetite and promote utilisation of food; secondly, where there is anorexia and loss of weight, as may occur after prolonged fevers, and in chronic wasting diseases.

To supplement the diet in partial deficiencies, a daily dose of 0·4 gramme of the concentrate is suggested. In the case of infants and young children, 0·1 gramme or more, according to age, could be given daily. It may be dissolved and mixed in the baby's feedings, if so desired. In serious conditions (beri-beri and late sprue), a daily dosage of 4 grammes (half-a-teaspoonful), or even larger doses, of 'RYZAMIN-B' could be given with safety, as excess of B vitamin orally has never been found toxic.

'RYZAMIN-B' is a clear, golden-brown, syrupy preparation, quite palatable and readily taken by children. A consistently high Vitamin B_1 potency is assured by bio-assay. The product is issued by Burroughs Wellcome & Co. in collapsible metal tubes of 15 grammes (with special tip), from which the desired quantity can be expressed. A special measuring spoon is issued with each tube.

VITAMIN C

A diet deficient in Vitamin C results in the development of scurvy both in man and animals. Scurvy develops gradually with loss of weight, listlessness, anæmia with hæmorrhages into the mucous membranes and skin, œdema and osteoporetic condition of the bones. Infantile scurvy is a relatively modern condition. In 1894, Barlow

* *Journal American Medical Association*, Maurice B. Strauss and William J. McDonald, 100:1320 (April), 1933.

described a disease of infants (scurvy-rickets) which is known to be a complication of rickets with a Vitamin C deficiency. The anti-scorbutic value of both cows' milk and human milk falls to a low level in many modern systems of diet. It is possible that Vitamin C may, in time, be proved to be an interesting exception to the generalisation that animals are unable to synthesise vitamins. Rats and pigeons, when fed on a diet deficient in Vitamin C, grow and reproduce in an approximately normal manner and scurvy does not develop. There is some reason to believe that the necessary amount of this vitamin may be produced by these animals. Man and the guinea-pig are relatively very susceptible to lack of Vitamin C.

Ascorbic Acid

It has been shown that the anti-scorbutic properties of fresh fruit and vegetables are due to the presence of a substance at one time believed to be "hexuronic acid," but now known to be hexuronic acid less a molecule of water and recently renamed ascorbic or cevitamic acid. It has been isolated as a fine crystalline substance from peppers, oranges, lemons, cabbages and other vegetable sources, and also from the cortex of the suprarenal gland. It has also been produced synthetically and is now available as 'Tabloid' Ascorbic Acid.

Vitamin D

As a result of extensive experimental work, it is now established that exposure of ergosterol, a sterol occurring in certain natural fats, to ultra-violet light gives rise to a product—irradiated ergosterol—having a very intense antirachitic activity. Irradiated ergosterol by treatment with dinitrobenzoyl chloride, gives a mixture of dinitro-esters from which calciferyl dinitro-benzoate can be separated. The latter, on hydrolysis, forms the pure crystalline antirachitic principle

with a constant activity of 40,000 units per mgm. The pure substance is known as calciferol and is used for the preparation of 'TABLOID' CALCIFEROL.

CAROTENE

The yellow pigment contained in many foodstuffs used for animal-feeding experiments in vitamin investigation was early associated with Vitamin A activity. This yellow pigment is seen typically in carrots, and hence its name—Carotene—although it is widely distributed throughout the vegetable kingdom. The relation between Vitamin A and the carotinoid pigments was only revealed when investigations offered fresh evidence of the Vitamin A activity of Carotene. Since this discovery established that Carotene exhibits the characteristic physiological properties of Vitamin A, it has been adopted as the international standard for Vitamin A.*

CALCIUM REQUIREMENTS

During pregnancy or lactation the administration of calcium is essential when it is considered that the dietary calcium is insufficient to meet the demands of the growing fœtus or infant. There is ample evidence to suggest that the normal absorption of calcium can proceed only if there is an adequate supply of Vitamin D, which appears to prevent the calcium from being precipitated in an insoluble form. It is probable that deficiency of Vitamin D renders the intestinal contents more alkaline than normal, and in this manner interferes with the absorption of the calcium. Further, if the amount of Vitamin D is inadequate and calcium is administered in excess, the calcium-phosphorus balance is upset and the absorption of both substances is impaired.

* Report of League of Nations Commission on Biological Standardisation No. CH 1055 (1) 1932.

TRADE MARK 'TABLOID' BRAND CALCIUM GLUCONATE

CALCIUM GLUCONATE [$Ca(C_6H_{11}O_7)_2.H_2O$] is a calcium salt of gluconic acid, containing approximately 9 per cent. of calcium. It may be administered whenever calcium therapy is indicated. The calcium, which is in combination with the relatively weak gluconic acid, is presented in an ideal condition for proper calcium metabolism.

'TABLOID' BRAND CALCIUM GLUCONATE, gr. 20 *(Chocolate-flavoured Base)*, consists of pure calcium gluconate combined with a suitable quantity of chocolate as flavouring. It is readily absorbed and does not upset the digestion. It does not increase the lactate content of the blood, but furnishes gluconic acid which is metabolised like sugar. Each product should be masticated and a glassful of water taken immediately afterwards. To ensure adequate absorption of the calcium ion, the product should be taken during the interdigestive periods when the intestinal reaction is least alkaline.

TRADE MARK 'TABLOID' BRAND CALCIUM GLUCONATE WITH CALCIFEROL

'TABLOID' BRAND CALCIUM GLUCONATE WITH CALCIFEROL presents Calcium Gluconate and Calciferol as an acceptable and easily assimilable combination. It not only ensures that the dietary calcium is sufficient for metabolic purposes, but provides a full Vitamin D content in the diet. The 'Tabloid' products should be masticated and a full glass of water taken immediately afterwards.

TRADE MARK 'TABLOID' BRAND CALCIUM GLUCONATE AND IRON (EFFERVESCENT)

During pregnancy or lactation, the combined administration of calcium and iron is essential when it is considered that the dietary calcium and

iron are insufficient to meet the demands of the growing fœtus or infant. In private practice and in ante-natal clinics, 'TABLOID' CALCIUM GLUCONATE AND IRON may be given with advantage, therefore, to pregnant women over long periods in order to ensure a sufficiency of calcium for bone formation and a sufficiency of iron to replace the abnormal loss of iron during pregnancy.

When dissolved in a tumblerful of water, it forms a palatable effervescent draught and, thus given, tends to increase the daily intake of water.

Dosage recommended in pre-natal cases is: one product in a tumblerful of water twice a day for a month. Treatment is resumed after lapse of another month and therafter as indicated. Alternatively, one product may be taken once a day during many months. For cases of suspected calcium and iron deficiency, one or two a day may be taken for prolonged periods. Larger doses may be given in districts where water is abnormally deficient in calcium salts.

TRADE MARK 'HYPOLOID' BRAND CALCIUM LÆVULATE

CALCIUM LÆVULATE is the calcium salt of lævulic acid, an acid obtained from glucose, lævulose and other sugars. The calcium content is relatively high, calcium lævulate containing 14·8 per cent. of calcium, or 50 per cent. more than calcium gluconate.

CALCIUM LÆVULATE is of particular value for intravenous injection, as ulceration or other undesirable effects do not appear to follow accidental extravasation. It has the further advantages that it is readily sterilised and is non-toxic in therapeutic doses.

'HYPOLOID' BRAND CALCIUM LÆVULATE is the preparation of choice for effective calcium medication by injection. It is a sterile, stable and non-irritating solution, and may be administered intramuscularly or subcutaneously in divided doses of 5 c.c. each, at different points, if the intravenous route is not practicable.

PREPARATIONS

TRADE MARK 'KEPLER' PRODUCTS

'KEPLER' COD LIVER OIL

Prices in London: Bottles of 8 *fl. oz.* (2/6) *and* 16 *fl. oz.* (4/0) *per bottle*

,, COD LIVER OIL WITH MALT EXTRACT

Prices in London: 2/1 *and* 3/8 *per bottle*

,, COD LIVER OIL WITH MALT EXTRACT AND CHEMICAL FOOD *(Phosphates Compound)* ... ... in bottles

Each fluid ounce contains: Iron Phosphate, gr. 2 [0·13 gm.]; Calcium Phosphate, gr. 3 [0·194 gm.]; Sodium Phosphate, gr. 1/4 [0·016 gm.]; and Potassium Phosphate, gr. 1/4 [0·016 gm.].

Price in London: 2/6 *per bottle*

,, COD LIVER OIL WITH MALT EXTRACT AND CREOSOTE ... ... in bottles

Each fluid ounce contains: Creosote, min. 4 [0·237 c.c.].

Price in London: 2/6 *per bottle*

,, COD LIVER OIL WITH MALT EXTRACT AND HYPOPHOSPHITES ... ... in bottles of two sizes

Each fluid ounce contains: Calcium Hypophosphite, gr. 4 [0·259 gm.]; Potassium Hypophosphite, gr. 2 [0·13 gm.]; and Sodium Hypophosphite, gr. 2 [0·13 gm.].

Prices in London: 2/6 *and* 4/7 *per bottle*

,, COD LIVER OIL WITH MALT EXTRACT AND IRON IODIDE ... ... in bottles

Each fluid ounce contains: Iron Iodide, gr. 2 [0·13 gm.].

Price in London: 2/6 *per bottle*

One teaspoonful to two dessertspoonfuls of any of the above 'Kepler' Cod Liver Oil combinations may be given, twice or thrice daily, after food

'KEPLER' MALT EXTRACT

Prices in London: 2/1 *and* 3/8 *per bottle*

,, WITH CHEMICAL FOOD *(Phosphates Compound)* in bottles

Each fluid ounce contains: Iron Phosphate, gr. 2 [0·13 gm.]; Calcium Phosphate, gr. 3 [0·194 gm.]; Sodium Phosphate, gr. 1/4 [0·016 gm.]; and Potassium Phosphate, gr. 1/4 [0·016 gm.].

Price in London: 2/6 *per bottle*

,, WITH GLYCEROPHOSPHATES ... in bottles of two sizes

Each fluid ounce contains: Calcium Glycerophosphate, gr. 4 [0·259 gm.]; Potassium Glycerophosphate, gr. 2 [0·13 gm.]; Sodium Glycerophosphate, gr. 2 [0·13 gm.]; and Magnesium Glycerophosphate, gr. 2 [0·13 gm.].

Prices in London: 2/6 *and* 4/7 *per bottle*

,, WITH HÆMOGLOBIN ... ... in bottles

Each fluid ounce contains: Hæmoglobin, gr. 8-3/4 [0·567 gm.].

Price in London: 2/6 *per bottle*

,, WITH HYPOPHOSPHITES ... in bottles of two sizes

Each fluid ounce contains: Calcium Hypophosphite, gr. 8 [0·518 gm.]; Potassium Hypophosphite, gr. 4 [0·259 gm.]; and Sodium Hypophosphite, gr. 4 [0·259 gm.].

Prices in London: 2/6 *and* 4/7 *per bottle*

TRADE MARK 'KEPLER' PRODUCTS—CONTINUED

'KEPLER' MALT EXTRACT WITH IRON IODIDE ... in bottles

Each fluid ounce contains: Iron Iodide, gr. 2 [0·13 gm.].

Price in London: 2/6 *per bottle*

,, WITH PEPSIN AND PANCREATIN ... ... in bottles

Each fluid ounce contains: Pure Pepsin and Pure Pancreatin, each, gr. 4 [0·259 gm.].

Price in London: 2/6 *per bottle*

One teaspoonful to two dessertspoonfuls of any of the above 'Kepler' Malt Extract combinations may be given, twice or thrice daily, with or immediately after food

VITAMIN CONCENTRATES

VITAMIN A

TRADE MARK 'TABLOID' BRAND CAROTENE, 0·002 gramme *(Sugar-coated)* [SEE LIST B. W. & Co.]

DIRECTION.—One to five products, according to age, three times a day.

Price in London: Bottles of 25 *at* 3/6 *per bottle*

VITAMIN B

TRADE MARK 'RYZAMIN-B' BRAND RICE POLISHINGS CONCENTRATE [SEE LIST B. W. & Co.]

DIRECTIONS.—*See pages* 22–24.

A special measuring spoon is issued with each tube

Price in London: Tubes of 15 *gm. (with Nozzle), at* 1/10 *per tube*

VITAMIN C

TRADE MARK 'TABLOID' BRAND ASCORBIC ACID, 0·005 gramme; and 0·025 gramme [SEE LIST B. W. & Co.]

DIRECTION.—One, or more, according to the severity of the condition.

Prices in London: 0·005 *gm., bottles of* 25 (2/0); 0·025 *gm., bottles of* 25 (4/6) *per bottle*

VITAMIN D

TRADE MARK 'TABLOID' BRAND CALCIFEROL, 0·0001 gramme (=4000 International Units); and 0·00025 gramme (=10,000 International Units) [SEE LIST B. W. & Co.]

DIRECTION.—One, or more, of the lesser strength, daily, as a prophylactic and as a supplement to cod liver oil in the treatment of rickets. In serious and intractable cases, the 0·00025 gm. strength is given once or twice daily. For administration to children, the products may be powdered in a little water or milk, or added to the child's food. Older children or adults may take the products with a draught of water.

Prices in London: 0·0001 *gm., bottles of* 25 (1/10) *and* 100 (5/11): 0·00025 *gm., bottles of* 25 (3/9) *and* 100 (13/2) *per bottle*

CALCIUM MEDICATION

TRADE MARK 'TABLOID' BRAND CALCIUM GLUCONATE, gr. 20 [1·296 gm.] *(Chocolate-flavoured Base)* [SEE LIST B. W. & Co.]

DIRECTIONS.—*For Adults*—two to three products, three times a day, before food. *For Children*—one product, three times a day, before food.

Price in London: Tubes of 25, *at* 1/10 *per tube*

TRADE MARK 'TABLOID' BRAND CALCIUM GLUCONATE WITH CALCIFEROL [SEE LIST B. W. & Co.]

Each contains: Calcium Gluconate, 0·325 gm., and Calciferol, 0·000025 gm. (1000 International Units Vitamin D in each product).

DIRECTION.—One, or more, to be taken with water, daily, as a prophylactic.

Prices in London: Bottles of 25 (1/10) *and* 100 (5/11) *per bottle*

TRADE MARK 'TABLOID' BRAND CALCIUM GLUCONATE AND IRON (EFFERVESCENT) [SEE LIST B. W. & Co.]

℞		
	Calcii Gluconatis,	gr. 20 [1·296 gm.]
	Ferri et Ammonii Citratis,	gr. 3 [0·194 gm.]
	Salis Effervescentis,	*q.s.*

DIRECTION.—One to two products, daily, in a tumblerful of water.

Price in London: Tubes of 20, *at* 2/1 *per tube*

TRADE MARK 'HYPOLOID' BRAND CALCIUM LÆVULATE, 1 gramme [gr. 15½ approx.], in 10 c.c. [SEE LIST B. W. & Co.]

DIRECTIONS.—*Adults*—10 c.c. may be given intramuscularly, intravenously or subcutaneously daily or every second day. *Children*—2 c.c. to 5 c.c., according to age, intramuscularly, intravenously or subcutaneously.

Price in London: Boxes of 5 *'Hypoloid' ampoules,* 5/6 *per box*

The words 'KEPLER,' 'TABLOID,' 'HYPOLOID' and 'RYZAMIN-B' are trade marks or brands

---

BURROUGHS WELLCOME & CO.
(THE WELLCOME FOUNDATION LTD.)
LONDON (ENG.)

Associated Houses:

NEW YORK MONTREAL SYDNEY CAPE TOWN MILAN
BOMBAY SHANGHAI BUENOS AIRES

Vitamin Content of Foods

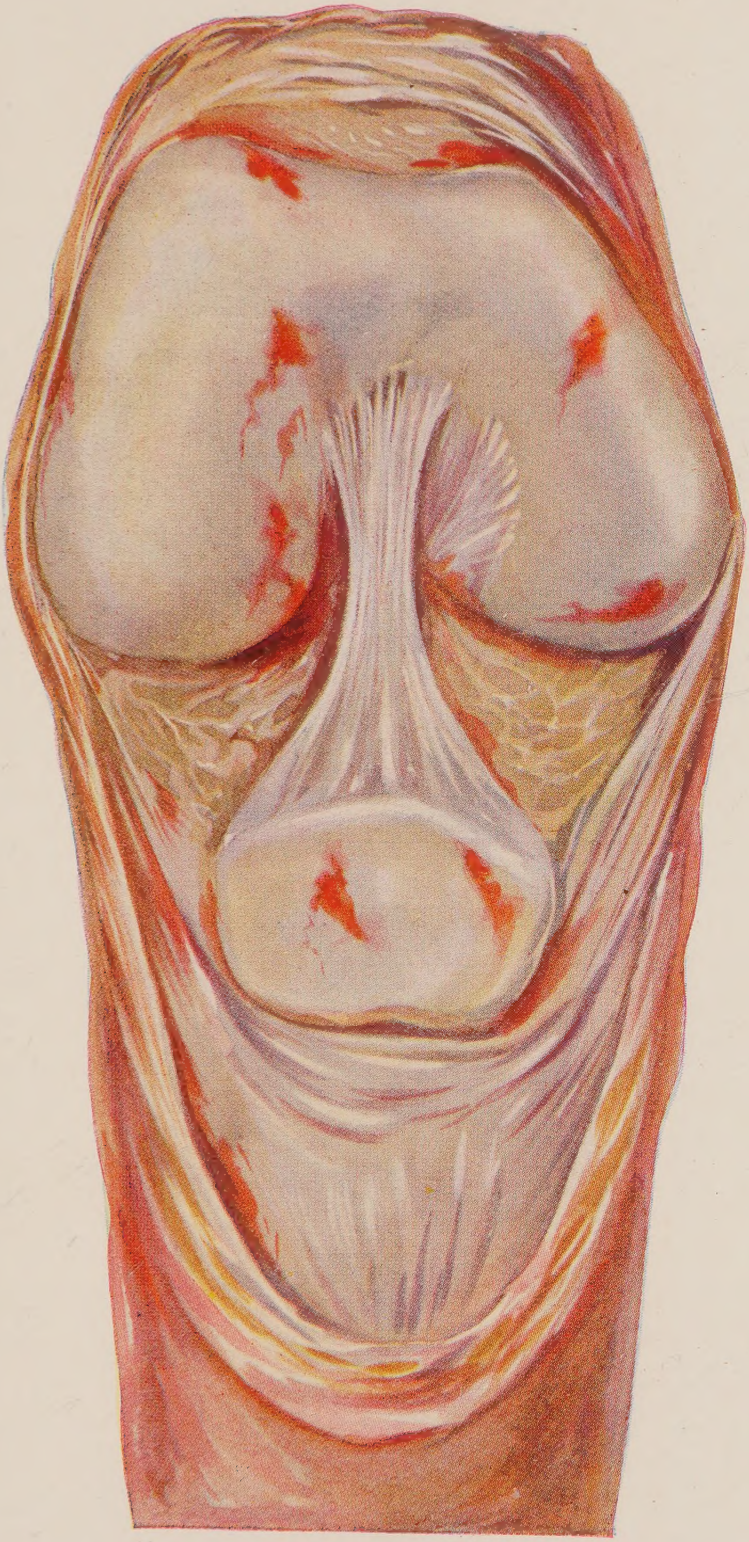
The following list shows the distribution of vitamins in the commoner foods: + indicates vitamin present, ++ good source, +++ rich source. B refers to the complex "water soluble" B, B_1 and B_2 being used where these have been separately estimated:—

Foods	Vitamins Contained
Beef	B_1++, B_2++, E++
Mutton	B_1++, B_2++
Liver, Ox	A+++, B_1++, B_2+++, E++
,, Pig	A+++, B++, C++, D+, E++
Heart, Ox	B_1++
,, Pig	B+, E++
Sweetbreads	A+, B++
Cod Liver Oil	A+++, D+++
Fish Roe	A++, B_1+
Egg yolk, Hen's	A++, B_1++, B_2+, D+++, E++
Milk, Cows' fresh	(varies) A+, B_1+, B_2++, C+, D+, E+
Butter, pasture	A++, D++, E++
Cheese, American Cheddar	A++, B_2+
,, skim milk	A+
Lard	Vitamins absent
Wheat-flour, wholemeal	A+, B_1+, B_2+
,, white	Vitamins absent
Beans, haricot	B_1++
,, kidney	A+, B++
Peas, dried	A+, B_1++, B_2++, C+
Potatoes, uncooked	A+, B_1++, B_2+, C+++
Carrot, raw (old)	A++, B_1++, B_2+, C+
Cabbage, green, fresh	A++, B_1++, B_2++, C+++, E+
Lettuce, green	A++, B_1++, B_2+, C+++, E+++
Tomato	A++, B++, B_1+, B_2+, C+++
Grape Fruit and Lemon	A+, B+, C+++
Orange Juice	A+, B+, C+++, E+

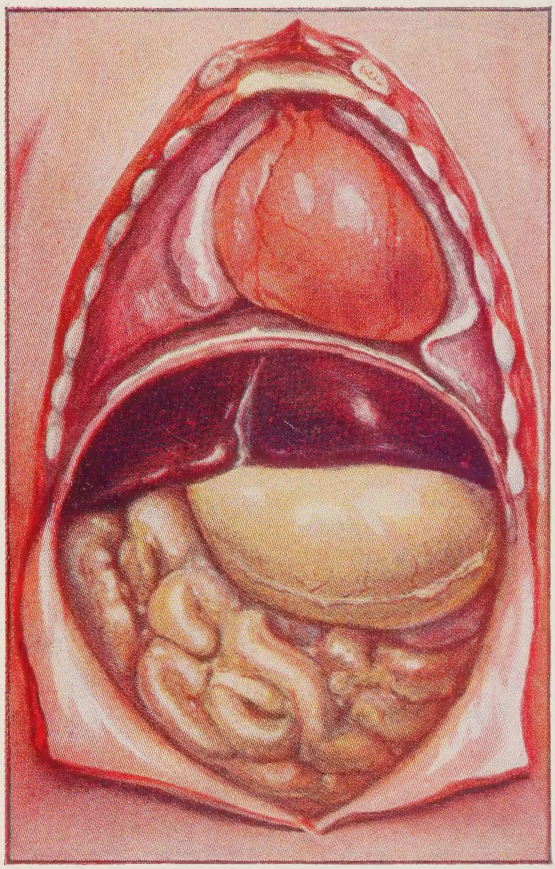
British Medical Research Council's Report, 1932

8092 *h/i/s/e/r* COPYRIGHT J. 5900

Raise flap of cover for further illustrations



Showing hæmorrhage into joint



INFANTILE BERI-BERI

Abdominal contents of an infant, showing characteristic pathological changes as a result of Vitamin B deficiency

Note enlarged liver, and dilated heart and stomach

PELLAGRA

VITAMIN DEFICIENCY
Typical pellagrous rash on the hand